## III. REMARKS

### Preliminary Remarks

Reconsideration and allowance of the present application based on the following remarks are respectfully requested. Claims 22-42 are currently pending and remain at issue in this application. This response is timely filed as it is accompanied by a petition for an extension of time to file in the third month and the requisite fee.

On page 2 of the official action, the examiner has acknowledged that the present application is a continuation of U.S. Patent Appl. No. 09/053,152. The examiner has requested that a specific reference to the earlier filed application be made in the instant application. The applicants have amended the specification by updating the priority information of the instant application including reference to U.S. Patent Appl. No. 09/053,152.

On page 3 of the official action, the examiner objected to the specification for lacking a brief description of the drawings section. The applicants hereby submit a section directed to a brief descriptions of the Figure 1. Specifically, the brief description is directed to the documented recordation of LH, FSH, $E_2$, and progesterone levels in a female patient both before and after cetrorelix treatment. Support for this amendment can be found throughout the specification, for example, Table II and page 10, lines 1-19. The applicants do not intend by these or any amendments to abandon subject matter of the claims as originally filed or later presented, and reserve the right to pursue such subject matter in continuing applications.

### Patentability Remarks

#### *Rejection Pursuant to 35 U.S.C. §112, Second Paragraph*

In paragraph 2 of the official action, the examiner rejected claims 22, 23, 26, 27, 29-32, 35, 37, 38, and 40 under 35 U.S.C. §112, second paragraph, for allegedly being indefinite. Specifically, the examiner asserted that the terms "LHRH antagonists, anti-estrogens, and LHRH agonist" in claims 22, 23, and 35 are vague. The examiner alleged that the specification's use of the language "such as" or "for example" does not explicitly define LHRH-antagonists, anti-estrogens, and LHRH agonists, but is merely exemplary. The examiner further alleged that the words "clomphencitrate" and "cetrorelix" lack insufficient antecedent basis in claims 26 and 27.

Solely to expedite prosecution and without prejudice to the applicants' right to seek broader claims in a continuing application, the applicants have canceled claims 23-25, and 35. Amended claim 22 is directed to a method of treating fertility disorders by administering an LHRH-antagonist selected from the group consisting of ganirelix, antarelix antide, azaline B, ramorelix, A-76154, Nal-Glu, 88-88 and cetrorelix, and inducing follicle growth by administration of hMG or recombinant FSH (controlled ovarian stimulation) in combination with the antiestrogen clomiphene, the improvement comprising administering an amount of said LHRH-antagonist which is sufficient to suppress endogenous LH while maintaining FSH secretion at a natural level and estrogen development is not affected until ovulation induction. Support for amended claim 22 can be found throughout the specification, for example on page 5, lines 2-7; page 7, lines 21 and 22; and page 10, lines 20 to page 11, line 15.

The applicants submit that the rejection regarding the use of the terms "antiestrogens" and "LHRH agonist" as presented in claims 23 and 35, is now moot as these claims have been canceled herein (without prejudice). With regard to the term "LHRH antagonist" in claim 22, the applicants have amended claim 22 to define the various LHRH antagonists that can be used to treat fertility disorders in the claimed invention.

The applicants further submit proper antecedent basis exists for dependent claims 26 and 27 with regard to the terms "cetrorelix" and "clomphencitrate." Specifically, both of the terms are now present in independent claim 22 from which claims 26 and 27 draw their dependency. Similarly, claims 29-32, 37, and 38 are ultimately dependent upon independent claim 22 and thus contain all of its' limitations. Dependent claim 40 has been amended to be directed to the method of claim 39, wherein Cetrorelix is administered beginning on cycle day 6 to 10 and ovulation is induced between day 7 and day 11 of the menstrual cycle. The term "Cetrorelix" has proper antecedent basis as dependent claim 40 draws its' dependency from independent claim 39.

In view of the foregoing amendment and remarks, the applicants respectfully request that the rejection of claims 22, 23, 26, 27, 29-32, 35, 37, 38, and 40 under 35 U.S.C. §112, second paragraph for being indefinite, has been overcome and should be withdrawn.

**Rejection Pursuant to 35 U.S.C. §102(a)**

In paragraph 6 of the official action, the examiner rejected claims 22, 24, 28-30, 36, 37, and 39-42 under 35 U.S.C. §102(a) as allegedly being anticipated by Oliveness *et al.*,

*Human Reproduction* 10:1382-1386 (1995; hereafter "Oliveness"). Specifically, the examiner alleged that Oliveness teaches a method of treating women with tubal factor-related infertility with the LHRH antagonist cetrorelix. The examiner further asserted that Oliveness teaches administering a cetrorelix dose on day 8 of the cycle, as well as a second dose 72 hours later. The examiner asserted that Oliveness further teaches that ovulation was triggered by administration of HCG, oocytes were retrieved and inseminated. Finally, the examiner alleged that Oliveness taught that LH plasma concentrations were decreased and FSH concentrations before and after cetrorelix did not show any noticeable modification.

As discussed above, amended claim 22 is directed to a method of treating female fertility disorders by administering an LHRH-antagonist selected from the group consisting of ganirelix, antarelix antide, azaline B, ramorelix, A-76154, Nal-Glu, 88-88 and cetrorelix, and inducing follicle growth by administration of hMG or recombinant FSH (Controlled Ovarian Stimulation) in combination with clomiphene. Amended claim 39 is directed to a method of treating infertility disorders comprising administering an amount of cetrorelix as an LH-RH antagonist which is sufficient to suppress endogenous LH while maintaining FSH secretion at a natural level and not affecting estrogen development and further administrating an antiestrogen consisting of clomiphene for inducing follicle growth, wherein after cessation of cetrorelix administration, subsequent follicle development is facilitated only with remaining endogenous LH and FSH.

The applicants submit that the examiner has acknowledge that methods for treating female fertility disorders by administering an LHRH-antagonist (*e.g.*, cetrorelix) in combination with an antiestrogen (*e.g.*, clomphencitrate) is free of the prior art (see Official Action, page 7, paragraph 7 last paragraph). Oliveness *et al.* neither teach nor suggest co-administration of an LHRH-antagonist and an antiestrogen to treat infertility disorders. Specifically, Oliveness *et al.* did not report the administration of LHRH antagonists (in single, dual, or multiple doses) for the prevention of a premature LH surge in combination with clomiphene, and HMG or FSH for ovarian stimulation. Also, Oliveness *et al.* do not teach further administration of native LHRH, recombinant LH, or LHRH agonists like HCG for inducing ovulation and preventing ovarian hyperstimulation syndrome. Dependent claims 28, 29, 30, 36, 37, and 40-42 draw their limitations from either claims 22 or 39, and are thus not anticipated by Oliveness *et al*'s teachings. As discussed above, claim 24 has been canceled without prejudice. In view of the foregoing amendment and remarks, the applicants

respectfully submit that the rejection of claims 22, 24, 28-30, 36, 37, and 39-42 under 35 U.S.C. §102(a) as allegedly being anticipated by Oliveness *et al.* has been overcome and should be withdrawn.

**Rejection Pursuant to 35 U.S.C. §103(a)**

In paragraph 7 of the official action, the examiner rejected claims 33-35 and 38 under 35 U.S.C. §103(a) as allegedly being obvious over Oliveness. Specifically, the examiner asserted that although Oliveness does not specifically disclose inducing ovulation with LHRH agonists or native LHRH to reduce ovarian hyperstimulation syndrome, this modification would be obvious because the administration of these agents along with cetrorelix may be advantageous to reduce the occurrence of ovarian hyperstimulation syndrome.

A *prima facie* case of obviousness requires: (1) some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) the teaching or suggestion of all the claim limitations of the applicants' invention in the combined prior art references; and (3) a reasonable expectation of success. M.P.E.P. § 2143. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure." *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Moreover, the prior art must provide some teaching, suggestion or motivation to make the **specific** combination that was made by the applicant." *In re Dance*, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998) (emphasis added) (citing *In re Raynes*, 7 F.3d 1037, 1039, 28 USPQ2d 1630, 1631 (Fed. Cir. 1993); *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992).

As discussed above, claim 35 has been canceled without prejudice. The applicants respectfully submit that dependent claims 33, 34 and 38 draw their limitations from claim 22, which is directed to a method of treating fertility disorders by administering an LHRH-antagonist such as cetrorelix, and inducing follicle growth by administration of hMG or recombinant FSH. These therapeutic compounds are combined with an antiestrogen such as clomphencitrate to suppress an LH surge, and maintain natural levels of FSH and estrogen secretion. Oliveness *et al.* neither teach nor suggest administering an LHRH antagonist in

combination with an antiestrogen along with either hMG or recombinant FSH to (1) stimulate the ovaries for a controlled release of an egg, and yet (2) prevent premature ovulation, while (3) maintaining FSH and estrogen levels. One of skill in the art reading the teachings of Oliveness *et al.* would not have been motivated to use the antiestrogen in this combination treatment to improve female infertility. Accordingly, the applicants submit that Oliveness *et al.* neither teach nor suggest the applicants' claimed invention. In view of the foregoing amendment and remarks, a prima facie case of obviousness does not exist. Therefore, the rejection based on 35 U.S.C. §103(a) in view of Oliveness *et al.* of claims 33-35, and 38 has been overcome and should be withdrawn.

## III. CONCLUSION

In view of the foregoing, the applicants believe that the claims are in form for allowance, and hereby respectfully solicit such action. If any point remains in issue which the examiner feels may be best resolved through a personal or telephone interview, the examiner is strongly urged to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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